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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/718,295      | 11/21/2000  | Rui Mei              | 3359                | 2944             |

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EXAMINER

ALLEN, MARIANNE P

ART UNIT PAPER NUMBER

1631

DATE MAILED: 09/25/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/718,295

Applicant(s)

MEI ET AL.

Examiner

Marianne Allen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 14 May 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-39 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-39 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election in Paper No. 4 is acknowledged. However, upon further consideration of the subject matter, the restriction set forth in Paper No. 3 is hereby vacated. All claims have been examined in their entirety.

### ***Specification***

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See at least pages 19, 21, and 26.

### ***Drawings***

The formal drawings submitted 5/14/02 in combination with the corrected substitute formal drawings submitted 6/25/02 have been approved by the draftsman.

### ***Claim Rejections - 35 USC § 112***

Claims 1-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an enablement rejection.

Claim 1 requires "predicting hybridization intensities of a plurality of candidate probes."

The specification and at least claim 3 provides an equation to determine hybridization intensity. However, the value of the constant " $C_2$ " is not provided nor how to determine its value.

The value of the weight coefficient " $W_i$ " is not provided. The specification indicates that in some embodiments " $W_i$ " may be determined by multiple linear regression analysis but fails to provide what data is being analyzed. It is unknown how to determine " $W_i$ " for other embodiments encompassed. Page 16 indicates the values of " $W_i$ " in a physical model (note that the claims are not so limited) may be determined by empirical data. However, the specification does not appear to provide an explicit algorithm to arrive at " $W_i$ " values. Note that the information on page 19 is a particular multiple linear regression model with respect to a reference base such as A and that the claims are not limited to the simple hybridization scheme of Figure 4, the relationships set forth in Equations 4-8, or the necessity for a training data set from experimental data as disclosed on page 20. It is noted with respect to equation 8 that the assumption is that  $W_i = C_i P_i$  is not a limitation of the claims. It is noted that page 19, line 4, recites " $C_2$ " and this recitation does not appear to be associated with any equation. It is noted that the model for probes of N bases in length set forth on page 19, following equation 8, is confusing. Note that the subscripting notation does not correspond to the expansion of the summation in equation 8. In addition, the last line does not reflect the subscript "M" (i.e.  $\text{Ln}(I_M)$ ) but rather repeats the subscript "1" (i.e.  $\text{Ln}(I_1)$ ).

" $S_i$ " is stated to be "a functional of said sequence of said probe" in both the claims and specification. It is not known what this phrase means. If it should be a function of the probe, it is not known what that function is. Page 18 of the specification (with reference to Figure 5) provides a particular way to determine the value of " $S_i$ " based upon the sequence of the probe. No other methods to determine this value are disclosed.

Claim 1 further requires “predicting quantitative responses of said candidate probes to the amount of their targets.” The specification on page 3 states that the quantitative response is the slope of the response curve of a probe. However, how the response curve is determined is not set forth. Pages 17-22 discuss interactions of probes (“P”) to targets (“T”) in view of their concentration, but it is unclear what is considered the response curve of a probe from which to determine the slope and thus the quantitative response in view of the claims.

Claim 1 further requires “selecting said probes from said candidate probes according to said hybridization intensities and said quantitative response.” However, this recitation fails to provide the criteria by which a probe is selected or excluded. That is, the claim provides no cut-off value or other means to determine whether a probe would be selected or not. Note that the quality scores discussed on page 24 are not limitations of the claims. Note that the various modules discussed are with reference to unidentified co-pending applications which do not appear to be either issued or allowed applications. Note that at least page 2; page 16, line 14; page 17, line 20; page 24, line 21; page 25, line 16; and page 32, line 11, contain blanks for co-pending application numbers or other information. Applicant is cautioned against introducing new matter.

Claim 8 requires “filtering out a subset of said candidate probes, wherein said subset probes have apparent affinity constant above a threshold.” This provides a limitation for exclusion but not selection. It is unclear from the way the claim is written if all remaining probes are implicitly selected. Apparent affinity constants are discussed on pages 21-22, but no other methods of determining them are disclosed. It appears from page 22 that equation 12 is the basis for claims 8-11; however, the claims are not so limited.

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Note that claim 13 recites calculating a unified quality score based upon predicted hybridization intensities; however, the only portion of the specification discussing such scores is pages 25-26 and the claims are not limited to the particular way in which these unified quality scores were calculated.

Note that these comments are with respect to the perfect match hybridization intensity predictions but apply to the equations for predicting mismatch hybridization intensities for the same reasons. (See for example claims 5-7 and 12-13.)

The above remarks are addressed with respect to the methods of claims 1-13 but apply for the same reasons to the software of claims 14-25 and the system of claims 27-39.

The claims do not reflect the particular steps and multiple linear regression models used in the examples to achieve the goal of selecting oligonucleotide probes and no guidance is provided on other computer implemented methods for selecting oligonucleotide probes. The examples in the specification fail to provide sufficient information or guidance to permit one of ordinary skill in the art to reproduce them.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 703-308-0666. The examiner can normally be reached on Monday-Friday, 9:00 am - 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703-308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

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*Marianne P. Allen*

Marianne P. Allen

Primary Examiner

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September 18, 2002